REMARKS

Examiner Nguyen is thanked for courtesies extended during the March 11, 2003 telephone interview.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 20-33, 35-42, 47-49, 51-64, 67-85 and 87-103 are pending in this application. Claims 20, 21, 29, 30, 49, 54-56, 60, 62, 76-85, 89 and 90 have been amended; claims 91-103 have been added; claims 34, 43-46, 50, 65, 66 and 86 have been cancelled. Support for the recitation of "RRE-type sequence" in the amended and new claims can be found on page 7, line 4, of the specification.

The cross-reference to the parent application (now U.S. Patent No. 6,312,682) has been updated by amendment to the specification.

No new matter is added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

II. THE REJECTIONS UNDER 35 U.S.C. §112, 1ST PARAGRAPH ARE OVERCOME

Claims 20-90 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. The rejection is traversed.

The Office Action objected to the recitation of "functional equivalents" to describe systems that perform the same function as the *rev*/Rev responsive element (RRE) system. As discussed during the March 11, 2003 telephone interview, this term has been replaced by "one or more RRE-type sequences" to more clearly define the nature of the functional equivalents.

The Examiner points out one example of an RRE-type sequence, the constitutive transport element (CTE) found in Mason Pfizer monkey virus (MPMV), on page 2 of the Office Action. References to other RRE-type sequences can be found, for example, in the

accompanying reference by Tabernero *et al.* (1996). This reference was available before the earliest priority date of the current application, and discusses CTEs from simian retrovirus type 1 (SRV-1) and simian retrovirus type 2 (SRV-2), in addition to MPMV. Therefore, contrary to the statement on page 3 of the Office Action, knowledge in the prior art and a description as to the availability of a representative number of species are present. One skilled in the art, at the time the application was filed, would have recognized that other RRE-type sequences could perform the same function as the *rev*/RRE system, and that the Applicants were in possession of the claimed genus.

Claims 20-90 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is traversed.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988), determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors, for example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Undue experimentation is not required in this case. The quantity of experimentation required to substitute molecules containing RRE-type sequences for the *rev*/RRE system is low. Direction and examples showing how to make and use such a system are present in the specification. The state of the art is such that several RRE-type sequences which perform equivalently to the *rev*/RRE system are known and described; and, the level of skill in the art is high. One of skill in the art would be able to use the instant specification and the knowledge available in the art at the time the application was filed to produce a lentivirus-based retroviral vector particle comprising an RRE-type sequence. It would be well within the means of the skilled artisan to determine and evaluate an RRE-type sequence that enhances export of RNA transcripts of the vector genome from the nucleus to the cytoplasm of an infected cell.

In view of the amendments, arguments and telephone interview of March 11, 2003, reconsideration and withdrawal of the Section 112, first paragraph, rejections are requested.

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III. THE DOUBLE PATENTING REJECTION IS OVERCOME

Claims 20-90 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-71 of U.S. Patent No. 6,312,682. The issue of whether there is indeed double patenting is contingent upon whether the claims are allowed. Upon agreement as to allowable subject matter, if it is believed that there is still a double patenting issue, a Terminal Disclaimer will be filed at that time. Accordingly, it is requested that the double patenting rejection be held in abeyance until agreement is reached as to allowable subject matter.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

On page 1, line 2:

This is a Divisional Application of [allowed] United States Patent Application No. 09/224,014, now U.S. Patent No. 6,312,682, filed on December 28, 1998, which is a Continuing Application of PCT/GB97/02857, filed on October 17, 1997 and claiming priority to Great Britain Patent Application No. 9621680.9, filed on October 17, 1996, and Great Britain Patent Application No. 9624457.9, filed on November 25, 1996.

In the Claims:

20. (Amended) An infection and transduction competent, lentivirus-based retroviral vector particle comprising a genome, gag, pol, an envelope protein, and optionally one or more RRE-type sequences [a rev protein or functional equivalents thereof], wherein the particle lacks all functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof].

21. (Amended) An infection and transduction competent, lentivirus-based retroviral vector particle comprising a genome, gag, pol, [and]an envelope protein and one or more RRE-type sequences, wherein the particle lacks all functional lentiviral auxiliary gene products[; or the particle lacks all functional lentiviral auxiliary gene products, except a rev protein or functional equivalents thereof].

29. (Amended) A retroviral vector production system for producing the infection and transduction competent, lentivirus-based retroviral vector particle according to claim 20, which system comprises nucleic acid sequence(s) encoding the genome of the retroviral vector particle, gag, pol, and [the] an envelope protein, and optionally comprising one or more RRE-type sequences, wherein all functional lentiviral auxiliary proteins are absent from the retroviral particle[the rev protein or functional equivalents thereof, wherein all lentiviral auxiliary genes, or all lentiviral auxiliary genes except the optionally present *rev* or functional equivalents thereof, are absent or are disrupted, whereby functional auxiliary proteins encoded by said auxiliary genes are and not expressed in the system].

30. (Amended) A retroviral vector production system for producing infection and transduction competent, lentivirus-based vector particle according to claim 21, which system comprises nucleic acid sequence(s) encoding the genome of the vector particle, gag, pol, and an

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envelope protein, or the genome of the vector particle, gag, pol, an envelope protein, and comprising one or more RRE-type sequences, wherein all functional lentiviral auxiliary proteins are absent from the retroviral particle[a rev protein or functional equivalents thereof, wherein all lentiviral auxiliary genes, or all lentiviral auxiliary genes except *rev* or functional equivalents thereof, are absent or are disrupted, whereby functional auxiliary proteins encoded by said auxiliary genes are not expressed in the system].

49. (Amended) A set of nucleic acid sequences encoding the components of the infection and transduction competent, lentivirus-based vector particle according to [any one of claims] claim 20 [or 21], comprising: a first DNA construct which encodes the genome of the vector particle, a second DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes an envelope protein, wherein: one of the DNA constructs optionally comprises one or more RRE-type sequences [encodes a rev protein or functional equivalents thereof]; and all functional[other] lentiviral auxiliary gene products are absent from the retroviral vector particle [and producer cells in which the sequences are expressed, and lentiviral auxiliary genes encoding said other lentiviral auxiliary gene products are absent from or disrupted in the set of sequences].

54. (Amended) A method for producing the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 [or 21], comprising coexpressing in a retroviral producer cell nucleic acid sequence(s) encoding the genome of the vector particle, gag and pol proteins, and an envelope protein, and, optionally comprising RRE-type sequences [a rev protein or functional equivalents thereof; wherein one of the nucleic acid sequence(s) optionally encodes a rev protein or functional equivalents thereof]; and wherein all functional[other] lentiviral auxiliary gene products are absent from the retroviral vector particle [and producer cells in which the sequence(s) are expressed, and lentiviral auxiliary genes encoding said other lentiviral auxiliary gene products are absent from or disrupted in the sequence(s)].

55. (Amended) A method for producing the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 or 21, comprising coexpressing in a retroviral producer cell nucleic acid sequence(s) encoding the genome of the vector particle, gag and pol proteins, and an envelope protein; wherein all functional lentiviral auxiliary gene products are absent from the retroviral vector particle [and producer cells in which

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the sequence(s) are expressed, and lentiviral auxiliary genes encoding said lentiviral auxiliary gene products are absent from or disrupted in the sequence(s)].

56. (Amended) A method for producing the infection and transduction competent, lentivirus-based, replication defective vector particle according to claim 20 [or 21], consisting essentially of coexpressing in a retroviral producer cell nucleic acid sequence(s) encoding the genome of the vector particles, gag and pol proteins, and an envelope protein.

60. (Amended) The method of claim 54 wherein the coexpressing is of: a first DNA construct which encodes the genome of the vector particles, a second DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes the envelope protein, wherein one of the DNA constructs optionally comprises one or more RRE-type sequences [encodes a rev protein or functional equivalents thereof].

62. (Amended) The method of claim 56 wherein the coexpressing is of: a first DNA construct which encodes the genome of the vector particles, a second DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes the envelope protein, wherein one of the DNA constructs optionally comprises one or more RRE-type sequences [encodes a rev protein or functional equivalents thereof].

76. (Amended) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 54, wherein the particle lacks all functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof].

77. (Amended) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 55, wherein the particle lacks all functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof].

78. (Amended) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 56, wherein the particle lacks all functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof].

79. (Amended) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 57, wherein the particle lacks all

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functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof].

80. (Amended) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 58, wherein the particle lacks all functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof].

81. (Amended) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 59, wherein the particle lacks all functional lentiviral auxiliary gene products [other than the optionally present rev protein or functional equivalents thereof the optionally present rev protein or functional equivalents thereof].

82. (Amended) An isolated nucleic acid sequence encoding the components of the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 [or 21], comprising DNA construct(s) which encode the genome of the vector particle, gag and pol proteins, and an envelope protein, wherein, the nucleic acid sequence produces the lentivirus-based, replication defective vector particle, and, wherein: the DNA construct(s) optionally comprise one or more RRE-type sequences [encode a rev protein or functional equivalents thereof]; and all [other] functional auxiliary gene products are absent from the retroviral vector particle [and producer cells in which the nucleic acid sequence is expressed, and are also absent from or disrupted in the nucleic acid sequence].

83. (Amended) Isolated nucleic acid sequence(s) encoding the components of the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 or 21, comprising construct(s) which encode the genome of the vector particle, gag and pol proteins, and an envelope protein, wherein all functional auxiliary gene products[, or all functional auxiliary gene products except rev protein or functional equivalents thereof,] are absent from the retroviral vector particle [and producer cells in which the nucleic acid sequence(s) is/are expressed and are absent from or disrupted in the sequence(s)].

84. (Amended) Isolated nucleic acid sequence(s) encoding the components of the infection and transduction competent, lentivirus-based vector particle of claim 20 [or 21], consisting essentially of construct(s) which encode(s) the RNA genome of the vector particle,

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gag and pol proteins, and an envelope protein, wherein the construct(s) optionally comprises one or more RRE-type sequences [encode(s) rev or functional equivalents thereof].

85. (Amended) The retroviral vector production system wherein according to claim 29 or 30 wherein the retroviral vector particle is based on HIV-1 and auxiliary genes *vpu*, *vpr*, *vif, tat, rev* and *nef* are absent or are disrupted.

89. (Amended) The retroviral vector production system [wherein] according to claim 29 or 30 wherein at least one RRE-type sequence comprises [is rev or functional equivalents thereof is present as] a constitutive transport element (CTE).

90. (Amended) The retroviral particle of claim 20 or 21 wherein at least one RRE-type sequence comprises [is rev or functional equivalents thereof is present as] a constitutive transport element (CTE).